

EPIDEMIOLOGY BULLETIN

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August, 1985

Volume 85, Number 8

Recommendations for Protection Against Viral Hepatitis

Recommendation of the Immunization Practices Advisory Committee (ACIP) of the U.S. Public Health Service

The following statement updates all previous recommendations on use of immune globulins for protection against viral hepatitis and use of hepatitis B vaccine and hepatitis B immune globulin for prophylaxis of hepatitis B.

ntroduction

The term "viral hepatitis" is commonly used for several clinically similar diseases that are etiologically and epidemiologically distinct (1). Two of these, hepatitis A (formerly called infectious hepatitis) and hepatitis B (formerly called serum hepatitis) have been recognized as separate entities since the early 1940s and can be diagnosed with specific serologic tests. The third, currently known as non-A, non-B hepatitis, is probably caused by at least two different agents, and lacking specific diagnostic tests, remains a disease diagnosed by exclusion. It is an important form of acute viral hepatitis in adults and currently accounts for most post-transfusion hepatitis in the United States. An epidemic type of non-A, non-B hepatitis, which is probably spread by the fecal-oral route and is different from the types seen in the United States, has been described in parts of Asia and North Africa (2).

A fourth type of hepatitis, delta hepatitis, has recently been characterled as an infection dependent on hepatitis B virus. It may occur as a coinfection with acute hepatitis B infection or as superinfection of a hepatitis B carrier (3).

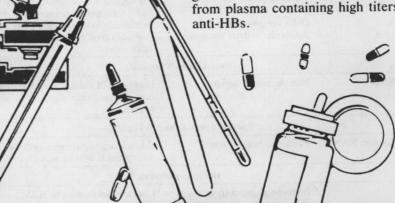
Hepatitis Surveillance

Approximately 21,500 cases of hepatitis A, 24,300 cases of hepatitis B, 3,500 cases of non-A, non-B hepatitis, and 7,100 cases of hepatitis type unspecified were reported in the United States in 1983. Most cases of each type occur among young adults. Since reporting from many localities is incomplete, the actual number of hepatitis cases occurring annually is thought to be several times the reported number.

Immune Globulins

Immune globulins used in medical practice are sterile solutions of antibodies (immunoglobulins) from human plasma. They are prepared by cold ethanol fractionation of large plasma pools and contain 10%-18% protein. In the United States, plasma is primarily obtained from professional donors. Only plasma shown to be free of hepatitis B surface antigen (HBsAg) is used to prepare immune globulins.

Immune globulin (IG) (formerly called "immune serum globulin," ISG, or "gamma globulin") produced in the United States contains antibodies against the hepatitis A virus (anti-HAV) and the hepatitis B surface antigen (anti-HBs). Tests of IG lots prepared since 1977 indicate that both types of antibody have uniformly been present. Hepatitis B immune globulin (HBIG) is an IG prepared from plasma containing high titers of anti-HBs.



Neither IG nor HBIG commercially available in the United States transmits hepatitis or other viral infections. There is no evidence that the causative agent of AIDS (human T-lymphotropic virus type III/lymphadenopathy-associated virus [HTLV-III/ LAVI) has been transmitted by IG or HBIG (4).

Serious adverse effects from immune globulins administered as recommended have been exceedingly rare. Standard immune globulins are prepared for intramuscular use and should not be given intravenously. Two preparations for intravenous use in immunodeficient and other selected patients have recently become available in the United States but are not

recommended for hepatitis prophylaxis. Immune globulins are not contraindicated for pregnant women.

Hepatitis A

Hepatitis A is caused by the hepatitis A virus (HAV), a 27-nm ribonucleic acid (RNA) agent that is a member of the picornavirus family. The illness caused by HAV characteristically has an abrupt onset with fever, malaise, anorexia, nausea, abdominal discomfort, and jaundice. Severity is related to age. In children, most infections are asymptomatic, and illness is usually not accompanied by jaundice. Most infected adults become symptomatically ill with jaundice. Fatality among reported cases is infrequent

The incubation period of hepatitis A is 15-50 days (average 28-30). High

Hepatitis A is primarily transmitted

by person-to-person contact, gener-

ally through fecal contamination,

Transmission is facilitated by poo

personal hygiene, poor sanitation, and

intimate (intrahousehold or sexual)

contact. Common-source epidemics

from contaminated food and water

also occur. Sharing utensils or ciga-

rettes or kissing are not believed to

transmit the infection.

(about 0.6%).

concentrations of HAV (108 particles/ g) are found in stools of infected persons. Fecal virus excretion reaches its highest concentration late in the incubation period and early in the prodromal phase of illness, and diminishes rapidly once jaundice appears. Greatest infectivity is during the 2-week period immediately before the onset of jaundice. Viremia is of short duration; virus has not been found in urine or other body fluids. A chronic carrier state with HAV in blood or feces has not been demonstrated. Transmission of HAV by blood transfusion has occurred but is rare.

The diagnosis of acute hepatitis A is confirmed by finding IgM-class anti-HAV in serum collected during tl acute or early convalescent phase of disease. IgG-class anti-HAV, which appears in the convalescent phase of disease and remains detectable in serum thereafter, apparently confers enduring protection against disease. Commercial tests are available to detect IgM anti-HAV and total anti-HAV in serum.

Although the incidence of hepatitis A in the United States has decreased over the last 15 years, it is still a common infection in older children and young adults. About 38% of reported hepatitis cases in this country are attributable to hepatitis A.

Recommendations for IG prophylaxis of hepatitis A. Numerous field studies conducted in the past 4 decades confirm that IG given before exposure or during the incubation period of hepatitis A is protective against clinical illness (5-7). Its prophylactic value is greatest (80%-90%) when given early in the incubation period and declines thereafter (7).

Preexposure prophylaxis. The major group for whom preexposure propl laxis is recommended is international travelers. The risk of hepatitis A for U.S. citizens traveling abroad varies with living conditions, incidence of

TABLE 1. Hepatitis nomenclature

Abbreviation	Term	Comments				
	Hepatitis	A				
HAV	Hepatitis A virus	Etiologic agent of "infectious" hepatitis; a				
Anti-HAV	Antibody to HAV	picornavirus; single serotype. Detectable at onset of symptoms; lifetime persistence.				
IgM anti-HAV	IgM class antibody to HAV	Indicates recent infection with hepatitis A positive up to 4-6 months after infection.				
On the soling	Hepatitis	Bind red to be proper your ballions.				
нву	Hepatitis B virus	Etiologic agent of "serum" or "long- incubation" hepatitis; also known as Dane particle.				
HBsAg	Hepatitis B surface antigen	Surface antigen(s) of HBV detectable in large quantity in serum; several subtypes identified.				
HBeAg	Hepatitis B e antigen	Soluble antigen; correlates with HBV replication, high titer HBV in serum, and infectivity of serum.				
HBcAg Anti-HBs	Hepatitis B core antigen Antibody to HBsAg	No commercial test available. Indicates past infection with and immunity to HBV, passive antibody from HBIG, or immune response from HBV vaccine.				
Anti-HBe	Antibody HBeAg	Presence in serum of HBsAg carrier sug- gests lower titer of HBV.				
Anti-HBc Antibody to HBcAg Indicates past infection with H undefined time.						
IgM anti-HBc	IgM class antibody to HB- cAg	Indicates recent infection with HBV; positive for 4-6 months after infection.				
DAMES IN THE PARTY	Delta hepa	titis				
δ virus	Delta virus	Etiologic agent of delta hepatitis; may only cause infection in presence of HBV.				
δ-Ag Anti-δ	Delta antigen Antibody to delta antigen	Detectable in early acute delta infection. Indicates past or present infection with delta virus.				
	Non-A, non-B	hepatitis				
NANB	Non-A, non-B hepatitis	Diagnosis of exclusion. At least two candidate viruses; epidemiology parallels that of hepatitis B.				
Y Washington	Epidemic non-A, no	on-B hepatitis				
Epidemic NANB	Epidemic non-A, non-B hepatitis	Causes large epidemics in Asia, North Africa; fecal-oral or waterborne.				
	Immune glo	bulins				
IG	Immune globulin (previously ISG, immune serum globulin,	Contains antibodies to HAV, low titer antibodies to HBV.				
HBIG	or gamma globulin) Hepatitis B immune globulin	Contains high titer antibodies to HBV.				

hepatitis A infection in areas visited, and length of stay (8,9). In general, travelers to developed areas of western Europe, Japan, and Australia are at no greater risk of infection than in the United States. In contrast, travelers to developing countries may be at significant risk of infection. In such areas, the best way to prevent hepatitis A and other enteric diseases is to avoid potentially contaminated water or food. Drinking water (or beverages with ice) of unknown purity and eating uncooked shellfish or uncooked fruits or vegetables that are not peeled (or prepared) by the traveler should be avoided.

IG is recommended for travelers to developing countries if they will be eating in settings of poor or uncertain sanitation (some restaurants or homes) or will be visiting extensively with local persons, especially young children, in settings with poor sanitary conditions. Persons who plan to reside in developing areas for long periods should receive IG regularly if they anticipate exposure as described above or will be living in rural areas with poor sanitation.

For such travelers, a single dose of IG of 0.02 ml/kg is recommended if ravel is for less than 2 months. For prolonged travel, 0.06 ml/kg should be given every 5 months. For persons who require repeated IG prophylaxis, screening for total anti-HAV antibodies before travel may be useful to define susceptibility and eliminate unnecessary doses of IG in those who are immune.

Postexposure prophylaxis. A serologic test for the diagnosis of acute hepatitis A is now widely available. Since only 38% of acute hepatitis cases in the United States result from hepatitis A, serologic confirmation of hepatitis A in the index case is recommended before treatment of contacts. Serologic screening of contacts for anti-HAV before giving IG is not recommended because screening is more costly than IG and would delay its administration.

IG should be given as soon as possible after exposure; giving IG more than 2 weeks after exposure is not indicated.

Specific recommendations for IG prophylaxis of hepatitis A depend on the nature of the HAV exposure:

 Close personal contact. IG is recommended for all household and sexual contacts of persons with hepatitis A.

- 2. Day-care centers. Day-care facilities with children in diapers can be important settings for HAV transmission (10-12). IG should be administered to all staff and attendees of day-care centers or homes if: (a) one or more hepatitis A cases are recognized among children or employees; or (b) cases are recognized in two or more households of center attendees. When an outbreak (hepatitis cases in three or more families) occurs, IG should also be considered for members of households whose diapered children attend. In centers not enrolling children in diapers, IG need only be given to classroom contacts of an index case.
- 3. Schools. Contact at elementary and secondary schools is usually not an important means of transmitting hepatitis A. Routine administration of IG is not indicated for pupils and teachers in contact with a patient. However, when epidemiologic study clearly shows the existence of a school- or classroom-centered outbreak, IG may be given to those who have close personal contact with patients.

 Institutions for custodial care. Living conditions in some institutions, such as prisons and facilities for the developmentally

- disabled, favor transmission of hepatitis A. When outbreaks occur, giving IG to residents and staff who have close contact with patients with hepatitis A may reduce the spread of disease. Depending on the epidemiologic circumstances, prophylaxis can be limited in extent or can involve the entire institution.
- 5. Hospitals. Routine IG prophylaxis for hospital personnel is not indicated. Rather, sound hygienic practices should be emphasized. Staff education should point out the risk of exposure to hepatitis A and emphasize precautions regarding direct contact with potentially infective materials (13).

Outbreaks of hepatitis A among hospital staff occur occasionally, usually in association with an unsuspected index patient who is fecally incontinent. Large outbreaks have occurred among staff and family contacts of infected infants in neonatal intensive-care units. In outbreaks, prophylaxis of persons exposed to feces of infected patients may be indicated.

6. Offices and factories. Routine IG administration is not indicated under the usual office or factory conditions for persons exposed to a fellow worker with hepatitis A. Experience shows



that casual contact in the work setting does not result in virus transmission.

7. Common-source exposure. IG might be effective in preventing foodborne or waterborne hepatitis A if exposure is recognized in time. However, IG is not recommended for persons exposed to a common source of hepatitis infection after cases have begun to occur in those exposed, since the 2-week period during which IG is effective will have been exceeded.

If a foodhandler is diagnosed as having hepatitis A, commonsource transmission is possible but uncommon. IG should be administered to other foodhandlers but is usually not recommended for patrons. However, IG administration to patrons may be considered if (a) the infected person is directly involved in handling, without gloves, foods that will not be cooked before they are eaten; (b) the hygienic practices of the foodhandler are deficient; and (c) patrons can be identified and treated within 2 weeks of exposure. Situations where repeated exposures may have occurred, such as in institutional cafeterias, may warrant stronger consideration of IG use.

For postexposure IG prophylaxis, a single intramuscular dose of 0.02 ml/kg is recommended.

Hepatitis B

Hepatitis B virus (HBV) infection is a major cause of acute and chronic hepatitis, cirrhosis, and primary hepatocellular carcinoma worldwide. The frequency of HBV infection and patterns of transmission vary markedly in different parts of the world. In the United States, western Europe, and Australia, it is a disease of low endemicity, with only 0.1%-0.5% of the population being virus carriers and infection occurring primarily during adulthood. In contrast, HBV infection is highly endemic in China and Southeast Asia, sub-Saharan Africa, most Pacific islands, and the Amazon Basin; in these areas, 5%-15% of the population carry the virus, and most persons acquire infection at birth or during childhood. In other parts of the world, HBV is moderately endemic, and 1%-4% of persons are HBV carriers. Recommendations for prophylaxis of hepatitis B will vary in accordance with local patterns of HBV transmission. The recommendations that follow are intended for use in the United States.

Hepatitis B infection is caused by the HBV, a 42-nm, double-shelled deoxyribonucleic acid (DNA) virus. Several well-defined antigen-antibody systems have been associated with HBV infection (Table 1). HBsAg, formerly called "Australia antigen" or "hepatitis-associated antigen," is found on the surface of the virus and on accompanying 22-nm spherical and tubular forms. HBsAg can be identified in serum 30-60 days after exposure to HBV and persists for variable periods. The various subtypes (adr, adw, ayw, ayr) of HBsAg provide useful epidemiologic markers. Antibody against HBsAg (anti-HBs) develops after a resolved infection and is responsible for long-term immunity. Anti-HBc, the antibody to the core antigen (an internal component of the virus), develops in all HBV infections and persists indefinitely. IgM anti-HBc appears early in infection and persists for 6 or more months; it is a reliable marker of acute or recent HBV infection. The hepatitis B e antigen (HBeAg) is a third antigen, presence of which correlates with HBV replication and high infectivity. Antibody to HBeAg (anti-HBe) develops in most HBV infections and correlates with lower infectivity.

The onset of acute hepatitis B is generally insidious. Clinical symptoms and signs include various combinations of anorexia, malaise, nausea, vomiting, abdominal pain, and jaundice. Skin rashes, arthralgias, and arthritis can also occur. Overall fatality rates for reported cases generally do not exceed 2%. The incubation period of hepatitis B is long—45-160 days (average 60-120).

HBV infection in the United States. The estimated lifetime risk of HBV infection in the United States varies from almost 100% for the highest-risk groups to approximately 5% for the population as a whole. An estimated 200,000 persons, primarily young adults, are infected each year. Onequarter become ill with jaundice; more than 10,000 patients require hospitalization; and an average of 250 die of fulminant disease each year. Between 6% and 10% of young adults with HBV infection become carriers. The United States currently contains an estimated pool of 500,0001,000,000 infectious carriers. Chronic active hepatitis develops in over 25% of carriers and often progresses to cirrhosis. Furthermore, HBV carriers have a risk of developing primary liver cancer that is 12-300 times higher than that of other persons. It is estimated that 4,000 persons die from hepatitis B-related cirrhosis each year in this country and that more than 800 die from hepatitis B-related liver cancer.

The role of the HBV carrier is central in the epidemiology of HBV transmission. A carrier is defined as a person who is HBsAg-positive on at least two occasions at least 6 months apart. Although the degree of infectivity is best correlated with HBeAg-positivity, any person positive for HBsAg is potentially infectious. The likelihood of developing the carrier state varies inversely with the age at which infection occurs. During the perinatal period, HBV transmitted from HBeAgpositive mothers results in HBV carriage in up to 90% of infected infants, whereas 6%-10% of acutely infected adults become carriers.

Carriers and persons with acute infection have highest concentrations of HBV in the blood and serous fluids; less is present in other body fluids such as saliva and semen. Transmission occurs via percutaneous or permucosal routes. Infective blood or body fluids can be introduced by contaminated needles or through sexual contact. Infection can occur in settings of continuous close personal contact, such as in households or among children in institutions for the mentally retarded, presumably via inapparent or unnoticed contact of infectious secretions with skin lesions or mucosal surfaces. Transmission of infection by transfusion of contaminated blood or blood products has been greatly reduced since the advent of routine screening with highly sensitive tests for HBsAg. HBV is not transmitted via the fecal-oral route or by contamination of food or water.

Serologic surveys demonstrate that, although HBV infection is uncommon among adults in the general population, it is highly prevalent in certain groups. Those at risk, based on the prevalence of serologic markers of infection, are described in Table 2. Immigrants/refugees an their descendants from areas of high HBV endemicity are at high risk of acquiring HBV infection. Homosexually active men and users of illicit

TABLE 2. Prevalence of hepatitis B serologic markers in various population groups

Population group	Prevalence of serologic markers of HBV infection			
	HBsAG (%)	All markers (%)		
High risk				
Immigrants/refugees from areas of high				
HBV endemicity	13	70-85		
Clients in institutions for the mentally				
retarded	10-20	35-80		
Users of illicit parenteral drugs	7	60-80		
Homosexually active men	6	35-80		
Household contacts of HBV carriers	3-6	30-60		
Patients of hemodialysis units	3-10	20-80		
Intermediate risk				
Health-care workers—frequent blood				
contact	1-2	15-30		
Prisoners (male)	1-8	10-80		
Staff of institutions for the mentally		leusealleuithev.		
retarded	1	10-25		
Low risk				
Health-care workers—no or infrequent				
blood contact	0.3	3-10		
Healthy adults (first-time volunteer blood				
donors)	0.3	3-5		

injectable drugs are among the highest-risk groups, acquiring infection soon after adopting these lifestyles (10%-20%/year). Inmates of prisons lave high prevalence of HBV markers usually because of prior parenteral drug abuse; actual risk of transmission in prisons is also associated with parenteral drug abuse in prisons. Patients and staff in custodial institutions for the mentally retarded are also at increased risk of having HBV infection. Classroom contacts, particularly teachers or instructors, of some deinstitutionalized carriers may also be at higher risk than the general population. Household contacts and sexual partners of HBV carriers are at increased risk, as are hemodialysis patients and recipients of certain pooled plasma products.

There is increased risk for medical and dental workers and related laboratory and support personnel who have contact with blood. Employment in a hospital without exposure to blood carries no greater risk than that for the general population.

Hepatitis B prophylaxis. Two types of products are available for prophylaxis against hepatitis B. Hepatitis B vaccine, licensed in 1981, provides acve immunization against HBV infection, and its use is recommended for both pre- and postexposure prophylaxis. IG products provide temporary, passive protection and are indicated

only in certain postexposure settings.

IG and HBIG. IG and HBIG contain different amounts of anti-HBs. IG is prepared from plasma that is not preselected for anti-HBs content. Since 1977, all lots tested have contained anti-HBs at a titer of at least 1:100 by radioimmunoassay (RIA). HBIG is prepared from plasma preselected for high-titer anti-HBs. In the United States, HBIG has an anti-HBs titer of higher than 1:100,000 by RIA. There is no evidence that the causative agent of AIDS (HTLV-III/LAV) has been transmitted by IG or HBIG (4).

Hepatitis B vaccine. Hepatitis B vaccine licensed in the United States is a suspension of inactivated, alum-adsorbed 22-nm surface antigen particles that have been purified from human plasma by a combination of biophysical (ultracentrifugation) and biochemical procedures. Inactivation is a threefold process using 8M urea, pepsin at pH 2, and 1:4000 formalin. These treatment steps have been shown to inactivate representatives of all classes of viruses found in human blood, including the causative agent of AIDS (HTLV-III/LAV) (14). HB vaccine contains 20 µg/ml of HBsAg protein.

After a series of three intramuscular doses of hepatitis B vaccine, over 90% of healthy adults develop protective antibody (15,16). A course of three 10-µg doses induces antibody in

virtually all infants and children from birth through 9 years of age. The deltoid (arm) is the recommended site for hepatitis B vaccination in adults; immunogenicity of vaccine in adults is significantly lower when injections are given in the buttock (81%) (17). The immunogenicity of the intradermal route has not yet been clearly established.

Field trials of the U.S.-manufactured vaccine have shown 80%-95% efficacy in preventing infection or hepatitis among susceptible persons (16,18). Protection against illness is virtually complete for persons who develop adequate antibody levels* after vaccination. The duration of protection and need for booster doses are not yet defined. However, only 10%-15% of persons who develop adequate antibody after three vaccine doses will lose antibody within 4 years, and among those who lose antibody, protection against viremic infection and liver inflammation appears to persist. Immunogenicity and efficacy of the licensed vaccine in hemodialysis patients is much lower than in normal adults; protection may last only as long as adequate antibody levels persist (19).

Vaccine usage. Primary vaccination consists of three intramuscular doses of vaccine, with the second and third doses given 1 and 6 months, respectively, after the first. Adults and older children should be given 20 µg (1.0 ml) per dose, while children under 10 years should receive 10 µg (0.5 ml) per dose. For patients undergoing hemodialysis and for other immunosuppressed patients, a 40-µg (2.0-ml) dose should be used. Vaccine doses administered at longer intervals provide equally satisfactory protection, but optimal protection is not conferred until after the third dose. Hepatitis B vaccine should only be given in the deltoid muscle in adults and children or in the anterolateral thigh muscle in infants and neonates. Since hepatitis B vaccine is an inactivated (noninfective) product, it is presumed that there will be no interference with other simultaneously administered vaccines.

Data are not available on the safety of the vaccine for the developing fetus. Because the vaccine contains only noninfectious HBsAg particles,

^{*}Adequate antibody is 10 or more sample ratio units (SRU) by RIA or positive by enzyme immunoassay

there should be no risk to the fetus. In contrast, HBV infection in a pregnant woman may result in severe disease for the mother and chronic infection for the newborn. Pregnancy should not be considered a contraindication to the use of this vaccine for persons who are otherwise eligible.

Vaccine storage. Vaccine should be stored at 2 C-8 C (36 F-46 F) but not frozen. Freezing destroys the potency

of the vaccine.

Side effects and adverse reactions. The most common side effect observed in prevaccination trials was soreness at the injection site. Among an estimated 750,000 vaccinees, approximately 100 episodes of severe illness have been reported after receipt of vaccine. These have included arthralgias, neurologic reactions (such as Guillain-Barré syndrome), and other illnesses. The rate of Guillain-Barré syndrome following HB vaccine does not appear to be significantly increased above that observed in normal adults. Such temporally associated illnesses are not considered to be etiologically related to hepatitis B vaccine.

Effect of vaccination on carriers and immune persons. The vaccine produces neither therapeutic nor adverse effects in HBV carriers (20). Vaccination of individuals who possess antibodies against HBV from a previous infection is not necessary but will not cause adverse effects. Such individuals will have a postvaccination increase in their anti-HBs levels. Passively acquired antibody, whether from HBIG or IG administration or from the transplacental route, will not interfere with active immunization (21).

Prevaccination serologic screening for susceptibility. The decision to screen potential vaccine recipients for prior infection depends on three variables: (1) the cost of vaccination; (2) the cost of testing for susceptibility; and (3) the expected prevalence of immune individuals in the group. Figure I shows the relative cost-effectiveness of screening, given different costs of screening tests and the expected prevalence of immunity. In constructing the figure, the assumption was made that the cost of three doses of vaccine is \$100 and that there are additional costs for administration. For any combination of screening costs and immunity to hepatitis, the cost-effectiveness can be estimated. For example, if the expected

prevalence of serologic markers for HBV is over 20%, screening is costeffective if costs of screening are no greater than \$30 per person. If the expected prevalence of markers is less than 8%, and if the costs of screening are greater than \$10 per person, vaccination without screening is cost-effective.

Screening in groups with the highest risk of HBV infection (Table 2) will be cost-effective unless testing costs are extremely high. For groups at intermediate risk, cost-effectiveness of screening may be marginal, and vaccination programs may or may not utilize screening. For groups with a low expected prevalence of HBV serologic markers, such as health professionals in their training years, screening will not be cost-effective.

For routine screening, only one antibody test, either anti-HBc or anti-HBs, need be used. Anti-HBc will identify all previously infected persons, both carriers and noncarriers, but will not discriminate between members of the two groups. Anti-HBs will identify those previously infected, except carriers. For groups expected to have carrier rates of under 2%, such as health-care workers, neither test has a particular advantage. For groups with higher carrier rates, anti-HBc may be preferred to avoid unnecessary vaccination of carriers. If the RIA anti-HBs test is used for screening, a minimum of 10 RIA sample ratio units should be used to designate immunity (2.1 is the usual designation of a positive test). If enzyme immunoassay (EIA) is used, the manufacturers' recommended positive is appropriate.

Serologic confirmation of postvaccination immunity and revaccination of nonresponders. When given in the deltoid, hepatitis B vaccine produces protective antibody (anti-HBs) in more than 90% of healthy persons. Testing for immunity following vaccination is not recommended routinely but is advised for persons whose subsequent management depends on knowing their immune status, such as dialysis patients and staff, and for persons in whom a suboptimal response may be anticipated, such as those who have received vaccine in the buttock.

Revaccination of persons who do not respond to primary series (nonresponders) produces adequate antibody in only one-third when the primary vaccination has been given in the deltoid. Therefore, revaccination

of nonresponders to deltoid injection is not recommended routinely. For persons who did not respond to a primary vaccine series given in the buttock, preliminary data from two small studies suggest that revaccination in the arm induces adequate antibody in over 75%. Revaccination should be strongly considered for such persons.

Preexposure vaccination. Persons at substantial risk of acquiring HBV infection who are demonstrated or judged likely to be susceptible should be vaccinated. They include:

1. Health-care workers. The risk of health-care workers acquiring HBV infection depends on the frequency of exposure to blood or blood products and on the frequency of needlesticks. These risks vary during the training and working career of each individual but are often highest during the professional training period. For this reason, it is recommended that vaccination be completed during training in schools of medicine, dentistry,

nursing, laboratory technology,

and other allied health profes-

The risk of HBV infection for hospital personnel can vary both among hospitals and within hospitals. In developing specific immunization strategies, hospitals should use available published data about the risk of infection (22-24) and may wish to evaluate their own clinical and institutional experience with hepatitis B. Studies in urban centers have indicated that occupational groups with frequent exposure to blood and/or needles have the highest risk of acquiring HBV infection, including (but not limited to) the following groups: medical technologists, operating room staff, phlebotomists and intravenous therapy nurses, surgeons and pathologists, and oncology and dialysis unit staff. Groups shown to be at increased risk in some hospitals include: emergency room staff, nursing personnel, and staff physicians.

Other health-care workers based outside hospitals who have frequent contact with blood or blood products are also at in creased risk of acquiring HBV infection. These include (but are not limited to): dental professionals (dentists, oral surgeons,

- dental hygienists), laboratory and blood bank technicians, dialysis center staff, emergency medical technicians, and morticians.
- Clients and staff of institutions for the mentally retarded. Susceptible clients and staff who work closely with clients of institutions for the mentally retarded should be vaccinated. Risks for staff are comparable to those for health-care personnel in other high-risk environments. However, the risk in institutional environments is associated, not only with blood exposure, but also with bites and contact with skin lesions and other infective secretions. Susceptible clients and staff who live or work in smaller (group) residential settings with known HBV carriers should also receive hepatitis B vaccine.
- 3. Hemodialysis patients. Numerous studies have established the high risk of HBV transmission in hemodialysis units. Although recent data have shown not only adecrease in the rate of HBV infection in hemodialysis units but also a lower vaccine efficacy in these patients, vaccination is recommended for susceptible patients. Environmental control measures and regular serologic screening (based on immune status) of patients should be maintained.
- 4. Homosexually active men. Susceptible homosexually active men should be vaccinated regardless of their ages or duration of their homosexual practices. It is important to vaccinate persons as soon as possible after their homosexual activity begins. Homosexually active women are not at increased risk of sexually transmitted HBV infection.
- 5. Users of illicit injectable drugs.
 All users of illicit injectable drugs who are susceptible to HBV should be vaccinated as early as possible after their drug use begins.
- 6. Recipients of certain blood products. Patients with clotting disorders who receive clotting factor concentrates have an elevated risk of acquiring HBV infection. Vaccination is recommended for these persons and



should be initiated at the time their specific clotting disorder is identified. Screening is recommended for patients who have already received multiple infusions of these products.

7. Household and sexual contacts of HBV carriers. Household contacts of HBV carriers are at high risk of acquiring HBV infection. Sexual contacts appear to be at greatest risk. When HBV carriers are identified through routine screening of donated blood, diagnostic testing in hospitals, prenatal screening, screening of refugees, or other screening programs, they should be notified of their status and their susceptible household contacts vaccinated.

Families accepting orphans or accompanied minors from countries of high HBV endemicity should have the child screened for HBsAg, and if positive, family members should be vaccinated.

- 8. Other contacts of HBV carriers. Persons in casual contact with carriers at schools, offices, etc., are at minimal risk of acquiring HBV infection, and vaccine is not routinely recommended for them. However, classroom contacts of deinstitutionalized mentally retarded HBV carriers who behave aggressively or have special medical problems that increase the risk of exposure to their blood or serous secretions may be at risk. In such situations, vaccine may be offered to classroom contacts.
- Special high-risk populations.
 Some American populations, such as Alaskan Eskimos, native Pacific islanders, and immigrants and refugees from areas with highly endemic disease (particularly eastern Asia and sub-Saharan Africa) have high HBV infection rates. Depending on specific epidemiologic and pub

lic health considerations, more extensive vaccination programs should be considered.

- 10. Inmates of long-term correctional facilities. The prison environment may provide a favorable setting for the transmission of HBV because of the frequent use of illicit injectable drugs and homosexual practices. Moreover, it provides an access point for vaccination of parenteral drug abusers. Prison officials should consider undertaking screening and vaccination programs directed at those who abuse drugs before or while in prison.
- 11. Heterosexually active persons. Heterosexually active persons with multiple sexual partners are at increased risk of acquiring HBV infection; risk increases with increasing sexual activity. Vaccination should be considered for persons who present for treatment of sexually transmitted diseases and who have histories of sexual activity with multiple partners.

12. International travelers. Vaccination should be considered for persons who plan to reside more than 6 months in areas with high levels of endemic HBV and who will have close contact with the local population. Vaccination should also be considered for short-term travelers who are likely to have contact with blood from or sexual contact with residents of areas with high levels of endemic disease. Hepatitis B vaccination of travelers ideally should begin 6 months before travel in order to complete the full vaccine series; however, a partial series will offer some protection against HBV infection.

Postexposure prophylaxis for hepatitis B. Prophylactic treatment to prevent hepatitis B infection after exposure to HBV should be considered in the following situations: perinatal exposure of an infant born to an HBsAg-positive mother; accidental percutaneous or permucosal exposure to HBsAg-positive blood; or sexual exposure to an HBsAg-positive person.

Recent studies have established the relative efficacies of immune globulins and/or hepatitis B vaccine in various exposure situations. For perinatal exposure to an HBsAg-positive, HBeAg-positive mother, a regimen

combining one dose of HBIG at birth with the hepatitis B vaccine series started soon after bith is 85%-90% effective in preventing development of the HBV carrier state (25,27). Regimens involving either multiple doses of HBIG alone, or the vaccine series alone, have 70%-75% efficacy, while a single dose of HBIG alone has only 50% efficacy (28).

For accidental percutaneous exposure or sexual exposure, only regimens including HBIG and/or IG have been studied. A regimen of two HBIG doses, one given after exposure and one a month later, is about 75% effective in preventing hepatitis B following percutaneous exposure; a single dose of HBIG has similar efficacy when used following sexual exposure (29-31). IG may have some effect in preventing clinical hepatitis B following percutaneous exposures and can be considered as an alternative to HBIG when it is not possible to obtain HBIG.

Recommendations on postexposure prophylaxis are based on the efficacy data discussed above and on the likelihood of future HBV exposure of the person requiring treatment. In perinatal exposure and percutaneous exposure of high-risk health-care personnel, a regimen combining HBIG with hepatitis B vaccine will provide both short- and long-term protection, will be less costly than the two-dose HBIG treatment alone, and is the treatment of choice.

Perinatal exposure. One of the most efficient modes of HBV transmission is from mother to infant during birth. If the mother is positive for both HBsAg and HBeAg, about 70%-90% of infants will become infected, and up to 90% of these infected infants will become HBV carriers. If the HBsAg-positive carrier mother is HBeAg-negative, or if anti-HBe is present, transmission occurs less frequently and rarely leads to the HBV carrier state. However, severe acute

TABLE 3. Hepatitis B virus postexposure recommendations

Exposure	1	HBIG	Vaccine			
	Dose	Recommended timing	Dose	Recommended timing		
Perinatal	0.5 ml IM	Within 12 hours of birth	0.5 ml (10 μg) IM	Within 12 hours of birth*; repeat at 1 and 6 months		
Sexual	0.06 ml/kg IM	Single dose within 14 days of sexual contact	† state state a	Section Section 1		

^{*}The first dose can be given the same time as the HBIG dose but at a different

TABLE 4. Women for whom prenatal HBsAg screening is recommended

disease, including fatal fulminant hepatitis in the neonate, has been reported (32,33). Prophylaxis of infants from all HBsAg-positive mothers is recommended, regardless of th mother's HBeAg or anti-HBe status.

The efficacy of a combination of HBIG plus the hepatitis B vaccine series has been confirmed in recent studies. Although the following regimen is recommended (Table 3), other schedules have also been effective (25-27,34). The major consideration for all these regimens is the need to give HBIG as soon as possible after delivery.

HBIG (0.5 ml [10 µg]) should be administered intramuscularly after physiologic stabilization of the infant and preferably within 12 hours of birth. Hepatitis B vaccine should be administered intramuscularly in three doses of 0.5 ml (10 µg) each. The first dose should be given concurrently with HBIG but at a different site. If vaccine is not available at birth, the first vaccine dose may be given within 7 days of birth. The second and third doses should be given 1 month and 6 months, respectively, after the first. Testing for HBsAg and anti-HBs is recommended at 12-15 months to monitor the final success or failure therapy. If HBsAg is not detectable, and anti-HBs is present, the child has been protected. Testing for anti-HBc is not useful, since maternal anti-HBc may persist for more than 1 year; the utility of testing for IgM anti-HBc is currently being evaluated. HBIG administered at birth should not interfere with oral polio and diphtheriavaccines tetanus-pertussis administered at 2 months of age.

Maternal screening. Since efficacy of the treatment regimen depends on administering HBIG on the day of birth, it is vital that HBsAg-positive mothers be identified before delivery. Mothers belonging to groups known to be at high risk of acquiring HBV infection (Table 4) should be tested routinely for HBsAg during a prenatal visit. If a mother belonging to a highrisk group has not been screened prenatally, HBsAg screening should be done at the time of delivery, or as soon as possible thereafter, and the infant treated as above if the mother is HBsAg-positive. If the mother is identified as HBsAg-positive more than month after giving birth, the infanshould be screened for HBsAg, and if negative, treated with hepatitis B vaccine and HBIG.

[†]Vaccine is recommended for homosexual men and for regular sexual contacts of HBV carriers and is optional in initial treatment of heterosexual contacts of persons with acute HBV.

^{1.} Women of Asian, Pacific island, or Alaskan Eskimo descent, whether immigrant or U.S.-born.

^{2.} Women born in Haiti or sub-Saharan Africa.

^{3.} Women with histories of:

a. Acute or chronic liver disease.

b. Work or treatment in a hemodialysis unit.

c. Work or residence in an institution for the mentally retarded.

d. Rejection as a blood donor.

e. Blood transfusion on repeated occasions.

f. Frequent occupational exposure to blood in medico-dental settings.

g. Household contact with an HBV carrier or hemodialysis patient.

h. Multiple episodes of venereal diseases.

i. Percutaneous use of illicit drugs.

The appropriate obstetric and pediatric staff should be notified directly of HBsAg-positive mothers, so the staff may take appropriate precautions to protect themselves and other patients from infectious material, blood, and secretions, and so the neonate may receive therapy without delay after birth.

Acute exposure to blood that contains (or might contain) HBsAg. For accidental percutaneous or permucosal exposure to blood that is known to contain or might contain HBsAg, the decision to provide prophylaxis must take into account several factors: (1) the hepatitis B vaccination status of the exposed person; (2) whether the source of blood is known or unknown; and (3) whether the HBsAg status of the source is known or unknown. Such exposures usually occur in persons who are candidates for hepatitis B vaccine; for any exposure in a person not previously vaccinated, hepatitis B vaccination is recommended.

The following outline and table summarize prophylaxis for percutaneous (needlestick or bite), ocular, or mucous-membrane exposure to blood according to the source of exposure and vaccination status of the exposed person (Table 5). For greatest effectiveness, passive prophylaxis with HBIG (or IG) should be given as soon as possible after exposure (its value beyond 7 days of exposure is unclear).

1. Exposed person not previously vaccinated. Hepatitis B vaccination should be considered the treatment of choice. Depending on the source of the exposure, HBsAg testing of the source and additional prophylaxis of the exposed person may be warranted (see below). Screening the exposed person for immunity should be considered if such screening is cost-effective (as discussed in preexposure prophylaxis) and if this will not delay treatment beyond 7 days.

a. Source known HBsAg-positive. A single dose of HBIG (0.06 ml/kg) should be given as soon as possible after exposure and within 24 hours, if possible. The first dose of hepatitis B vaccine (20 μg) should be given intramuscularly at a separate site within 7 days of exposure, and the second and third doses given 1 month and 6 months later (Table 5)†. If HBIG cannot be

TABLE 5. Recommendations for hepatitis B prophylaxis following percutaneous exposure

	Exposed person					
Source	Unvaccinated	Vaccinated				
HBsAg-positive	HBIG x 1 immediately* Initiate HB vaccine† series.	Test exposed person for anti-HBs.§ If inadequate anti-body,¶ HBIG (x1) immediately plus HB vaccine booster dose.				
Known source High-risk HBsAg-positive	 Initiate HB vaccine series Test source for HBsAg. If positive, HBIG x 1. 	1. Test source for HBsAg only if exposed is vaccine nonresponder; if source is HBsAgpositive, give HBIG x 1 immediately plus HB vaccine booster dose.				
Low-risk HBsAg-positive	Initiate HB vaccine series.	Nothing required.				
Unknown source	Initiate HB vaccine series.	Nothing required.				

*HBIG dose 0.06 ml/kg IM.

†HB vaccine dose 20 µg IM for adults; 10 µg IM for infants or children under 10 years of age. First dose within 1 week; second and third doses, 1 and 6 months later.

§See text for details.

Less than 10 SRU by RIA, negative by EIA.

obtained, IG in an equivalent dosage (0.06 ml/kg) may provide some benefit.

b. Source known, HBsAg status unknown. The following guidelines are suggested based on the relative probability that the source is HBsAg-positive and on the consequent risk of HBV transmission.

(1) High risk that the source is HBsAg-positive, such as patients with a high risk of HBV carriage (Table 2) or patients with acute or chronic liver disease (serologically undiagnosed). The exposed person should be given the first dose of hepatitis B vaccine (20 µg) within 1 week of exposure and vaccination completed as recommended. The source person should be tested for HBsAg. If positive, the exposed person should be given HBIG (0.06 ml/kg) if within 7 days of exposure.

(2) Low risk that the source is positive for HBsAg. The exposed person should be given the first dose of hepatitis B vaccine (20 μg) within I week of exposure and vaccination completed as recommended. Testing of the source person is not necessary.

c. Source unknown. The exposed person should be given the first dose of hepatitis B vaccine (20 µg) within 7 days of exposure and vaccination completed as recommended.

2. Exposed person previously vaccinated against hepatitis B. For percutaneous exposures to blood in persons who have previously received one or more doses of hepatitis B vaccine, the decision to provide additional prophylaxis will depend on the source of exposure and on whether the vaccinated person has developed anti-HBs following vaccination.

†For persons who are not given hepatitis B vaccine, a second dose of HBIG should be given I month after the first dose.

- a. Source known HBsAg-positive. The exposed person should be tested for anti-HBs unless he/she has been tested within the last 12 months. If the exposed person has adequate antibody, no additional treatment is indicated.
 - (1) If the exposed person has not completed vaccination and has inadequate levels of antibody, one dose of HBIG (0.06 ml/kg) should be given immediately and vaccination completed as scheduled.
 - (2) If the exposed person has inadequate antibody on testing or has previously not responded to vaccine, one dose of HBIG should be given immediately and a booster dose of vaccine (1 ml or 20 μg) given at a different site.
 - (3) If the exposed person shows inadequate antibody on testing but is known to have had adequate antibody in the past, a booster dose of hepatitis B vaccine (1 ml or 20 μg) should be given.
- b. Source known, HBsAg status unknown.
 - (1) High risk that the source is HBsAg-positive. Additional prophylaxis is necessary only if the exposed person is a known vaccine nonresponder. In this circumstance, the source should be tested for HBsAg and, if positive, the exposed person treated with one dose of HBIG (0.06 ml/kg) immediately and a booster dose of vaccine (1 ml or 20 µg) at a different site. In other circumstances, screening of the source for HBsAg and the exposed person for anti-HBs is not routinely recommended, because the actual risk of HBV infection is very low (less than 1 per 1,000).¶
 - (2) Low risk that the source is HBsAg-positive. The risk of HBV infection is minimal. Neither testing of the source for HBsAg,



nor testing of the exposed person for anti-HBs, is recommended.

 Source unknown. The risk of HBV infection is minimal. No treatment is indicated.

Sexual contacts of persons with acute HBV infection. Sexual contacts of HBsAg-positive persons are at increased risk of acquiring HBV infection, and HBIG has been shown to be 75% effective in preventing such infections (31). Because data are limited, the period after sexual exposure during which HBIG is effective is unknown, but extrapolation from other settings makes it unlikely that this period would exceed 14 days. Prescreening sexual partners for susceptibility before treatment is recommended if it does not delay treatment beyond 14 days after last exposure. Testing for anti-HBc is the most efficient prescreening test to use in this population group.

A single dose of HBIG (0.06 ml/kg) is recommended for susceptible individuals who have had sexual contact with an HBsAg-positive person, if HBIG can be given within 14 days of the last sexual contact, and for persons who will continue to have sexual contact with an individual with acute hepatitis B before loss of HBsAg in that individual. In exposures between heterosexuals, hepatitis B vaccination may be initiated at the same time as HBIG prophylaxis; such treatment may improve efficacy of postexposure treatment. However, since 90% of persons with acute HBV infection become HBsAg-negative within 15 weeks of diagnosis, the potential for repeated exposure to HBV is limited. Hepatitis B vaccine is, therefore, optional in initial treatment for such exposures. If vaccine is not given, a second dose of HBIG should be given if the index patient remains HBsAgpositive for 3 months after detection. If the index patient is a known carrier or remains positive for 6 months, hepatitis B vaccine should be offered to regular sexual contacts. For exposures among homosexual men, the hepatitis B vaccine series should be initiated at the time HBIG is given. since hepatitis B vaccine is recommended for all susceptible homosexual men. Additional doses of HBIG are unnecessary if vaccine is given. IG is an alternative to HBIG when it is not possible to obtain HBIG.

Household contacts of persons with acute HBV infection. Prophylaxis for

other household contacts of persons with acute HBV infection is not indicated unless they have had identifiable blood exposure to the index case, such as by sharing toothbrushes or razors. Such exposures should be treated similarly to sexual exposures. If the index patient becomes a hepatitis B carrier, all household contacts should be given hepatitis B vaccine.

Delta Hepatitis

The delta virus (also known as hepatitis D virus [HDV] by some investigators) is a defective virus that may only cause infection in the presence of active HBV infection. The delta virus has been characterized as a particle of 35-37 nm in size, consisting of RNA (mw 500,000) as genetic material and an internal protein antigen (delta-antigen), coated with HBsAg as the surface protein (3). Infection may occur as either coinfection with hepatitis B or superinfection of a hepatitis B carrier, each of which usually cause an episode of acute hepatitis. Coinfection usually resolves, while superinfection frequently causes chronic delta infection and chronic active hepatitis. Both types of infection may cause fulminant hepatitis.

Delta infection may be diagnosed by detection of delta-antigen in serum during early infection and by the appearance of delta antibody during or after infection. Routes of delta transmission appear to be similar to those of hepatitis B. In the United States, delta infection occurs most commonly among persons at high risk of acquiring HBV infection, such as drug addicts and hemophilia patients.

A test for detection of delta antibody is expected to be commercially available soon. Other tests (delta antigen, IgM anti-delta) are available only in research laboratories.

Since the delta virus is dependent on hepatitis B for replication, prevention of hepatitis B infection, either preexposure or postexposure, will suffice to prevent delta infection in a person susceptible to hepatitis B. Known episodes of perinatal, sexual, or percutaneous exposure to sera or persons positive for both HBV and delta virus should be treated exactly as such exposures to hepatitis B alone.

Persons who are HBsAg carriers are at risk of delta infection, especially if they participate in activities that put them at high risk of repeated exposure to hepatitis B (parenteral drug abuse, homosexuality). How-

ever, at present there are no products available that might prevent delta infection in HBsAg carriers either before or after exposure.

Non-A, Non-B Hepatitis

United States. Non-A, non-B hepatitis that presently occurs in the United States has epidemiologic characteristics similar to those of hepatitis B, occurring most commonly following blood transfusion and parenteral drug abuse. Multiple episodes of non-A, non-B hepatitis have been observed in the same individuals and may be due to different agents. Chronic hepatitis following acute non-A, non-B hepatitis infection varies in frequency from 20% to 70%. Experimental studies in chimpanzees have confirmed the existence of a carrier state, which may be present in up to 8% of the population.

Although several studies have attempted to assess the value of prophylaxis with IG against non-A, non-B hepatitis, the results have been equivocal, and no specific recommendations can be made (35,36). However, for persons with percutaneous exposure to blood from a patient with non-A, non-B hepatitis, it may be reasonable to administer IG (0.06 ml/kg) as soon as possible after exposure.

Epidemic (fecal-oral) non-A, non-B hepatitis. In recent years, epidemics of non-A, non-B hepatitis spread by water or close personal contact have been reported from several areas of Southeast Asia (Indian subcontinent, Burma) and north Africa (2). Such epidemics generally affect adults and cause unusually high mortality in pregnant women. The disease has been transmitted to experimental animals, and candidate viruses have been identified; however, no serologic tests have yet been developed (37).

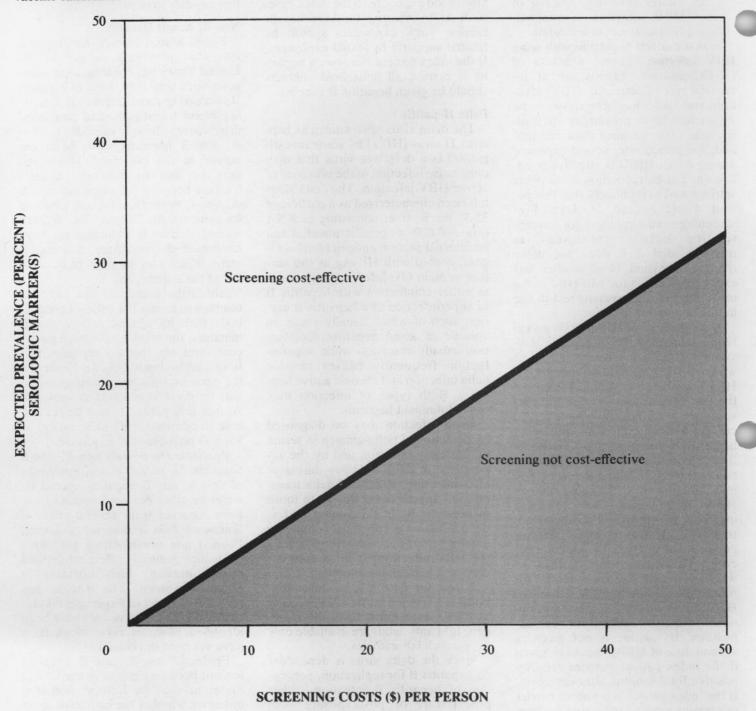
Epidemic non-A, non-B hepatitis has not been recognized in the United States or western Europe, and it is unknown whether the causative agent is present in these areas.

Travelers to areas having epidemic non-A, non-B hepatitis may be at some risk of acquiring this disease by close contact or by contaminated food

\$Adequate antibody is 10 SRU or more by RIA or positive by EIA.

^{**}Estimated by multiplying the risk of vaccine nonresponse in the exposed person (.10) by the risk of the needle source being HBsAg-positive (.05) by the risk of HBV infection in a susceptible person having an HBsAg-positive needlestick injury (.20).

FIGURE 1. Cost-effectiveness of prevaccination screening of hepatitis B virus vaccine candidates*



*See text for assumptions.

or water. The value of IG in preventing this infection is unknown. The best prevention of infection is to avoid potentially contaminated food or water, as with hepatitis A and other enteric infections.

References

- 1. Francis DP, Maynard JE. The transmission and outcome of hepatitis A, B, and non-A, non-B: a review. Epidemiol Rev 1979;1:17-31.
- Maynard JE. Epidemic non-A, non-B hepatitis. Seminars in Liver Disease 1984;4:336-9.
 Rizzetto M. The delta agent. Hepatology 1983;3:729-37.
- 4. CDC. Provisional public health service inter-agency recommendations for screening donated blood and plasma for antibody to the virus causing acquired immunodeficiency syndrome. MMWR 1985;34:1-5.
- 5. Kluge T. Gamma-globulin in the prevention of viral hepatitis. A study on the effect of mediumsize doses. Acta Med Scand 1963;174:469-77.

- Stokes J Jr, Neefe JR. The prevention and attenuation of infectious hepatitis by gamma globulin. Preliminary note. JAMA 1945;127:144-5.
- Mosley JW, Reisler DM, Brachott D, Roth D, Weiser J. Comparison to two lots of immune serum globulin for prophylaxis of infectious hepatitis. Am J Epidemiol 1968;87:539-50.
- Woodson RD, Cahill KM. Viral hepatitis abroad. Incidence in Catholic missionaries. JAMA 1972;219:1191-3.
- Woodson RD, Clinton JJ. Hepatitis prophylaxis abroad. Effectiveness of immune serum globulin in protecting Peace Corps volunteers. JAMA 1969;209:1053-8.
- Storch G, McFarland LM, Kelso K, Heilman CJ, Caraway CT. Viral hepatitis associated with day-care centers. JAMA 1979;242:1514-8.
- Hadler SC, Webster HM, Erben JJ, Swanson JE, Maynard JE. Hepatitis A in day-care centers. A community-wide assessment. N Engl J Med 1980;302:1222-7.
- Hadler SC, Erben JJ, Matthews D, Starko K, Francis DP, Maynard JE. Effect of immunoglobulin on hepatitis A in day-care centers. JAMA 1983;249:48-53.
- Favero MS, Maynard JE, Leger RT, Graham DR, Dixon RE. Guidelines for the care of patients hospitalized with viral hepatitis. Ann Intern Med 1979;91:872-6.
- ACIP. Hepatitis B vaccine: evidence confirming lack of AIDS transmission. MMWR 1984;33:685-7.
- Krugman S, Holley HP Jr, Davidson M, Simberkoff MS, Matsaniotis N. Immunogenic effect of inactivated hepatitis B vaccine: comparison of 20 microgram and 40 microgram doses. J Med Virol 1981;8:119-21.
- Szmuness W, Stevens CE, Harley EJ, et al. Hepatitis B vaccine: demonstration of efficacy in a controlled clinical trial in a high-risk population in the United States. N Engl J Med 1980;303:833-41.
- CDC. Suboptimal response to hepatitis B vaccine given by injection into the buttock. MMWR 1985;34:105-13.
- Francis DP, Hadler SC, Thompson SE, et al. The prevention of hepatitis B with vaccine. Report
 of the Centers for Disease Control multi-center efficacy trial among homosexual men. Ann
 Intern Med 1982;97:362-6.
- Stevens CE, Alter HJ, Taylor PE, Zang EA, Harley EJ, Szmuness W. Hepatitis B vaccine in patients receiving hemodialysis. Immunogenicity and efficacy. N Engl J Med 1984;311:496-501.
- Dienstag JL, Stevens CE, Bhan AK, Szmuness W. Hepatitis B vaccine administered to chronic carriers of hepatitis B surface antigen. Ann Intern Med 1982;96:575-9.
- Szmeness W, Stevens CE, Oleszko WR, Goodman A. Passive-active immunisation against hepatitis B: immunogenicity studies in adult Americans. Lancet 1981;1:575-7.
- Pattison CP, Maynard JE, Berquist KR, Webster HM. Epidemiology of hepatitis B in hospital personnel. Am J Epidemiol 1975;101:59-64.
- Dienstag JL, Ryan DM. Occupational exposure to hepatitis B virus in hospital personnel: infection or immunization? Am J Epidemiol 1982;115:26-39.
- Maynard JE. Viral hepatitis as an occupational hazard in the health care position. In: Vyas GN, Cohen SN, Schmid R, eds. Viral hepatitis. Philadelphia: Franklin Institute Press, 1978:321-31.
- Beasley RP, Hwang LY, Lee GC, et al. Prevention of perinatally transmitted hepatitis B virus infections with hepatitis B immune globulin and hepatitis B vaccine. Lancet 1983;2:1099-102.
- Wong VCW, Ip HMH, Reesink HW, et al. Prevention of the HBsAg carrier state in newborn infants of mothers who are chronic carriers of HBsAg and HBeAg by administration of hepatitis-B vaccine and hepatitis-B immunoglobulin: double-blind randomised placebo-controlled study. Lancet 1984;1:921-6.
- Stevens CE, Toy PT, Tong MJ, et al. Perinatal hepatitis B virus transmission in the United States. Prevention by passive-active immunization. JAMA 1985;253:1740-5.
- Beasley RP, Hwang LY, Stevens CE, et al. Efficacy of hepatitis B immune globulin for prevention of perinatal transmission of the hepatitis B virus carrier state: final report of a randomized double-blind, placebo-controlled trial. Hepatology 1983;3:135-41.
- Seeff LB, Wright EC, Zimmerman HJ, et al. Type B hepatitis after needle-stick exposure: prevention with hepatitis B immune globulin. Final report of the Veterans Administration Cooperative Study. Ann Intern Med 1978;88:285-93.
- Grady GF, Lee VA, Prince AM, et al. Hepatitis B immune globulin for accidental exposures among medical personnel: final report of a multicenter controlled trial. J Infect Dis 1978;138:625-38.
- Redeker AG, Mosley JW, Gocke DJ, McKee AP, Pollack W. Hepatitis B immune globulin as a prophylactic measure for spouses exposed to acute type B hepatitis. N Engl J Med 1975;293:1055-9.
- 32. Sinatra FR, Shah P, Weissman JY, Thomas DW, Merritt RJ, Tong MJ. Perinatal transmitted acute icteric hepatitis B in infants born to hepatitis B surface antigen-positive and anti-hepatitis Be-positive carrier mothers. Pediatrics 1982;70:557-9.
- Delaplane D, Yogev R, Crussi F, Shulman ST. Fatal hepatitis B in early infancy: the importance
 of identifying HBsAg-positive pregnant women and providing immunoprophylaxis to their
 newborns. Pediatrics 1983;72:176-80.
- Seeff LB, Koff RS. Passive and active immunoprophylaxis of hepatitis B. Gastroenterology 1984;86:958-81.
- Seeff LB, Zimmerman JH, Wright EL, et al. A randomized, double-blind controlled trial of the efficacy of immune serum globulin for the prevention of post-transfusion hepatitis. A Veterans Administration cooperative study. Gastroenterology 1977;72:111-21.
- Knodell RG, Conrad ME, Ginsburg AL, Bell CJ, Flannery EP. Efficacy of prophylactic gammaglobulin in preventing non-A, non-B post-transfusion hepatitis. Lancet 1976;1:557-61.
- Kane MA, Bradley DW, Shrestha SM, et al. Epidemic non-A, non-B hepatitis in Nepal. Recovery of a possible etiologic agent and transmission studies in marmosets. JAMA 1984;252:3140-5.

Cases of selected notifiable diseases, Virginia, for the period July 1 through July 31, 1985

	State				Regions					
Disease	This	Last			Mean 5 Year To Date	This Month				
Disease	Month	Month				N.W.	N.	s.w.	C.	E.
Measles	3	2	21	4	69	0	2	0	1	(
Mumps	3	7	31	14	46	0	0	2	0	
Pertussis	0	2	5	16	17	0	0	0	0	(
Rubella	1	0	2	_	11	0	0	1	0	
Meningitis—Aseptic	34	24	123	90	72	1	4	5	19	
*Bacterial	17	16	152	157	136	2	1	5	2	
Hepatitis A (Infectious)	7	14	108	62	106	1	0	1	1	
B (Serum)	50	63	340	285	293	5	9	13	12	1
Non-A, Non-B	9	11	59	58	38	2	1	3	1	100
Salmonellosis	131	230	882	649	701	14	24	23	40	3
Shigellosis	6	7	43	132	269	1	3	1	0	
Campylobacter Infections	77	102	373	320	169	21	15	11	14	10
Tuberculosis	7	42	220	244	_	_	_	_	_	-
Syphilis (Primary & Secondary)	18	23	173	240	334	0	1	0	7	10
Gonorrhea	1582	1924	10,638	11,133	11,742	_	_	_	_	_
Rocky Mountain Spotted Fever	7	7	15	26	39	2	0	2	1	100
Rabies in Animals	18	14	105	140	189	9	2	2	5	
Meningococcal Infections	5	4	40	43	48	1	1	1	2	1
Influenza	0	9	922	1095	1579	0	0	0	0	1
Toxic Shock Syndrome	1	0	1	6	5	0	0	1	0	
Reyes Syndrome	0	1	2	5	8	0	0	0	0	
Legionellosis	0	0	7	15	11	0	0	0	0	(
Kawasaki's Disease	0	1	21	9	13	0	0	0	0	
Other: Acquired Immunodeficiency Syndrome	13	7	45	15		1	7	0	1	

Counties Reporting Animal Rabies: Augusta 1 dog, 1 raccoon, 1 skunk; Bath 1 cat; Fauquier 1 groundhog, 3 raccoons, 1 cat; Fairfax 1 raccoon; Loudoun 1 red fox; Campbell 1 bat; Henry 1 bat; Hanover 1 bat, 1 raccoon; Henrico 1 bat; Richmond City 2 bats.

Occupational Illnesses: Carpal tunnel syndrome 21; Pneumoconiosis 18; Silicosis 5; Hearing loss 4; Asbestosis 3; Dermatoses 3; Poisoning, lead 2

Published Monthly by the VIRGINIA HEALTH DEPARTMENT Division of Epidemiology 109 Governor Street Richmond, Virginia 23219

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^{*}other than meningococcal